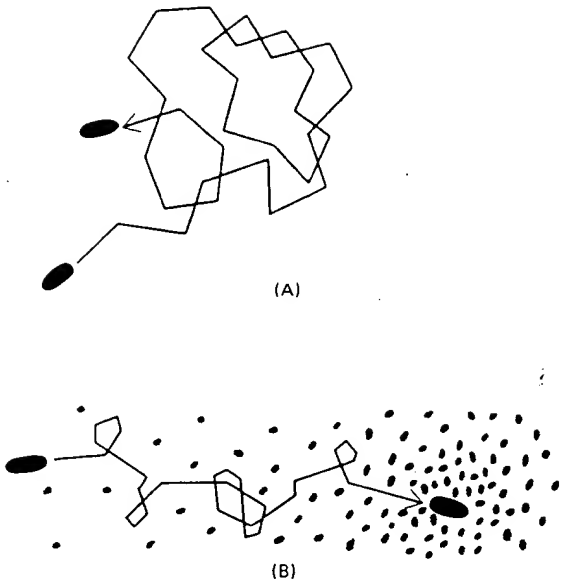

Figure 13–47 Schematic diagram of the tracks of a swimming bacterium. In the absence of a chemotactic signal (A), periods of smooth swimming are interrupted by brief tumbles that randomly change the direction of swimming. In the presence of a chemotactic attractant (B), tumbling is suppressed while the bacterium is swimming toward a higher concentration of the attractant so that it gradually moves in the direction of the attractant.

is an essential part of the chemotactic response, as it enables bacteria to respond to *changes* in concentration rather than to steady-state levels of an attractant and therefore to prolong swimming when moving in a favorable direction.

Chemotaxis-deficient Mutants Have Revealed Four Classes of Proteins Involved in Bacterial Chemotaxis[29]

The molecular mechanisms responsible for bacterial chemotaxis are being unraveled by the isolation and analysis of mutant bacteria defective in different aspects of chemotaxis. The mutants isolated so far fall into four broad classes that reflect the sequential flow of information from the cell-surface receptors to the flagellar motor.

The first class, the *specifically nonchemotactic* mutants, swim normally and respond to most chemotactic stimuli but are unable to respond to one specific chemical or group of closely related chemicals. The lesions in these mutants lie in 1 of the 20 or more genes encoding specific **periplasmic receptor proteins** that bind a specific chemical with high affinity. These receptor proteins are soluble and are found in the periplasmic space (between the outer membrane and the plasma membrane); they are the same proteins that help mediate the transport of specific chemicals across the plasma membrane (see p. 298). Although the transport and chemotaxis systems use a common initial receptor protein, the other parts of their machinery are different, as indicated by mutations that inactivate transport without affecting chemotaxis and vice versa.

The second class of mutants, the *multiply nonchemotactic* mutants, fail to respond to chemicals detected by several different cell-surface receptors but respond normally to chemicals detected by the remaining receptors. The lesions in these mutants involve one of three related transmembrane proteins, which are responsible for transmitting chemotactic signals across the plasma membrane. Because they become methylated during the chemotactic response (see below), they are known as **methyl-accepting chemotaxis proteins (MCPs).** Each MCP is activated by binding its own set of periplasmic receptor proteins: MCP I binds type I receptors; MCP II binds type II receptors; and MCP III binds type III receptors (Figure 13–48). When a bacterium is

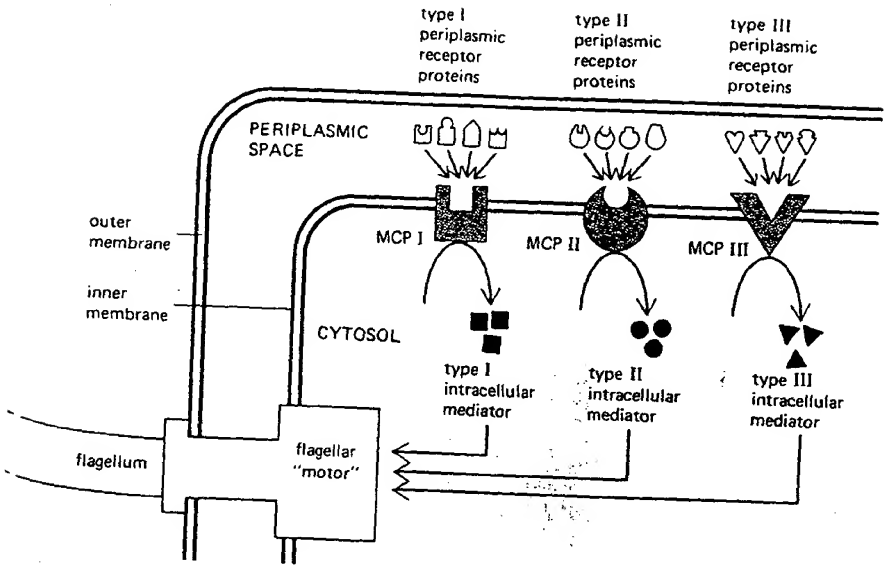

Figure 13–48 The steps in signal transduction during bacterial chemotaxis. Chemical attractants (not shown) bind to specific receptor proteins in the periplasmic space. The receptors then interact with one of three methyl-accepting chemotaxis proteins (MCPs) in the inner (plasma) membrane. The latter interaction activates the MCP to produce an intracellular mediator that causes the flagellar "motor" to continue to rotate counterclockwise, thereby suppressing tumbling and causing continuous smooth swimming. There are three sets of periplasmic receptor proteins (types I, II, and III), each of which interacts both with a specific small molecule and its own MCP. Although not shown in the figure, some chemical attractants directly bind to and activate an MCP; in such cases the MCP acts as both receptor and transducer.

exposed to a chemotactic attractant, the binding of the attractant induces a conformational change in the periplasmic receptor protein, causing the latter to bind to, and thereby activate, the appropriate MCP. The resulting activation of the MCP has two separable effects that correspond to the excitation and adaptation phases of the chemotactic response, respectively: (1) excitation occurs because the activated MCP generates an intracellular signal that causes the flagellar motor to continue to rotate counterclockwise, resulting in the suppression of tumbling and continuous smooth swimming; (2) adaptation occurs because the activated MCP can now be methylated by enzymes in the cytoplasm, reversing the activation of the MCP (see below).

The third class of mutants, the *generally nonchemotactic* mutants, fail to respond to any chemotactic stimuli. They have defects in one of eight different genes (proteins), including defects in the enzymes responsible for methylating (and demethylating) the MCPs and in other proteins required for relaying information between the receptors and the flagellar motor.

The final class of mutants, which also fail to respond to any chemotactic stimuli, are called *nonmotile* mutants. This class includes mutants with defects in 2 genes that control flagellar rotation and defects in 16 genes involved in the synthesis and assembly of flagella.

Protein Methylation Is Responsible for Adaptation[29]

There is compelling evidence that adaptation in bacterial chemotaxis results from the covalent methylation of the MCPs. When methylation is blocked by mutation, adaptation does not occur and exposure of the mutant bacteria to an attractant results in the suppression of tumbling for days instead of for minutes.

The methylation of MCPs is catalyzed by a soluble enzyme (*methyl transferase*) that transfers a methyl group from the common methyl group donor called *S-adenosylmethionine* to a free carboxyl group on a glutamic acid residue of the MCP (Figure 13–49). If an attractant is added that binds to a type I receptor, there is a large increase in the level of methylation of MCP I, while an attractant that binds to a type II or type III receptor induces the methylation of MCP II or MCP III, respectively. The methylation remains at this new level as long as the attractant is present. As many as four methyl groups can